TREATMENT OF CRANIOFACIAL DEFICITS ASSOCIATED WITH DOWN SYNDROME IN A MOUSE MODEL

Alexis N. Chom, Samantha L. Deitz (Randall J. Roper), Department of Biology, Indiana University-Purdue University Indianapolis, Indianapolis, Indiana, 46202

Trisomy 21 is the genetic source of the group of phenotypes commonly known as Down syndrome (DS). These phenotypes include cognitive impairment, heart defects and craniofacial abnormalities, including a small mandible. The Ts65Dn mouse model contains three copies of approximately half the genes found on human chromosome 21 and exhibits similar phenotypes to individuals with DS including a small, dysmorphic mandible. Our lab has traced this deficit to a smaller first branchial arch (BA1) consisting of fewer neural crest cells (NCCs) at embryonic day 9.5 (E9.5). At E9.5, Dyrk1a, a gene known to affect craniofacial development, is upregulated in the BA1, likely contributing to its cell deficit. Using epigallocatechin gallate (EGCG), an extract from green tea and a known inhibitor of Dyrk1a, we are attempting to rescue this deficit. We hypothesize the consumption of EGCG by pregnant mothers at E7 and E8 will rescue the mandibular deficit in developing embryos by reducing the expression or activity of Dyrk1a. From our data we conclude the treatment of pregnant mothers with EGCG results in increased embryo size of trisomic embryos. Further analysis will be done to determine embryo volume, the volume of the BA1, and number of NCCs within the BA1 to determine the effects of EGCG *in vivo*. This research will better our understanding of craniofacial development and could lead to potential genetic-based therapies in the future.

Funding for this project is provided by the CTSI TRAC1 PDT Pilot Grant Mechanism at IUPUI (to R.J.R).